National Cancer Advisory Board (NCAB)
Subcommittee on Clinical Investigations

Pooks Hill Marriott Hotel
5151 Pooks Hill Road
Bethesda, MD
December 5, 2016
6:00 – 7:30 p.m. EST

DRAFT SUMMARY

Subcommittee Members:
Dr. Peter Adamson, Chair
Dr. Jeff Abrams, Executive Secretary
Dr. Francis Ali-Osman
Dr. Deborah Bruner
Dr. Judy Garber
Dr. Elizabeth Jaffee
Dr. Beth Karlan
Dr. Electra Paskett
Dr. Nancy Raab-Traub
Dr. Mack Roach

Other Participants:
Dr. Troy Budd, Division of Cancer Prevention, NCI
Dr. William (Bill) Dahut, NCI
Dr. Carol Ferrans, BSA
Dr. Lori Henderson, NCI
Dr. Barry Kramer, NCI
Dr. Douglas Lowy, NCI
Dr. Worta McCaskill-Stevens, NCI
Dr. Sylvia Plevritis, Board of Scientific Advisors (BSA)
Dr. Sheila Prindiville, NCI
Dr. Martine Roussel, St. Jude Children's Research Hospital
Dr. Sudha Sivaram, NCI
Dr. Margaret Spitz, Baylor College of Medicine
Dr. David Tuveson, BSA
Dr. Asad Umar, NCI
Dr. Glendie Marcelin, The Scientific Consulting Group, Rapporteur

Opening Remarks

Dr. Peter Adamson, the new Subcommittee Chair, welcomed the meeting participants. He introduced the Executive Secretary, Dr. Jeff Abrams. Dr. Adamson noted that the last time the Subcommittee met was in 2012 and expressed the need to reconvene at this time to discuss new issues. Members of the NCAB and BSA and other participants introduced themselves.

Dr. Adamson mentioned that the last time the subcommittee met, the National Clinical Trials Network (NCTN) was in the formative phase. Dr. Abrams described the groups that were undergoing transition.

Implementation of New National Institutes of Health (NIH) Clinical Trial Reforms and Initiatives
Dr. Lori A. Henderson

Dr. Lori A. Henderson, Program Director at the National Institute of Biomedical Imaging and Bioengineering (NIBIB), NIH, updated the participants on the current activities to meet the new NIH requirements and the first series of reforms and initiatives. Through these, the NIH is addressing the current challenges in design efficiency and reporting of clinical trials, which would include such efforts as having a single Institutional Review Board (IRB) for multisite trials and investigators' using a clinical trial protocol template. She explained that the policies that have been released to the public are well defined, and others are still being revised. The new policies for NIH-funded trials stewardship include the following:

- Submitted applications from investigators must go through their specific Funding Opportunity Announcements (FOAs) for clinical trials.
- NIH Awardees must be trained in ICH (International Conference on Harmonization) Good Clinical Practice (GCP).
- GCP training is required for key NIH extramural staff involved in NIH-funded clinical trials.

Other policies that exist as guidance principles are focused on key elements and strategies to standardize project management, review or monitor trials, and identify and address barriers for staff or investigators. The overall goal of the NCI is to develop a comprehensive stewardship plan that is broad-based and encompasses conduct, oversight, and management of clinical trials, as well as to establish a solid foundation in the understanding of the current principles of GCP. Dr. Henderson mentioned an operational manual for NCI staff to "red tape" the policies and procedures and educational materials for investigators to standardize practices. The first chapter focuses on the mandatory GCP training of NCI staff. NCI staff may take any of several online courses as part of the training requirement. The second chapter focuses on the application requirements for clinical trials that must be submitted through specific FOAs. She went on to describe briefly the proposed categories of trial-specific information required for new FOA templates (e.g., NIH-required, optional, and recommended information).

Dr. Henderson reviewed the current parent grants (NCI-wide FOAs) and cautioned that a proposal that does not contain a clinical trial aim will be directed to standard R01 parent grant announcements. She concluded by outlining the next steps of the 10-month transition (ending on September 27, 2017), which includes a scientific review by the Division of Extramural Activities and developing NCI's clinical trial oversight and management procedures.

Discussion

A meeting participant asked for clarification of the NIH requirement for application submission. Dr. Henderson explained that applicants can no longer submit an application to the parent R01 grant mechanism, but rather must go through the specific funding announcement or clinical trial initiative for each Institute.

Dr. Electra Paskett raised a concern that the new requirements would provide extra work for investigators conducting behavioral and/or educational research and will prove difficult because of the lack of experience writing such protocols among this type of research community.

Dr. Deborah Bruner also expressed concern about these policies and asked for an explanation of the goal of the redesign of requirements. Dr. Abrams responded that this is an NIH initiative to ensure that clinical trials are monitored at a higher level than before. The NIH decided to become more "hands on," which was unexpected, but will provide additional information.

Dr. Mack Roach questioned the reason for the change and wondered if the decision, which creates more work, was based upon data observation. Dr. Douglas Lowy responded by saying that there was a concern that NIH staff were ill informed of their clinical trial portfolio.

Dr. Bruner reemphasized that the new requirements will not work for behavioral studies/research (e.g., health disparities).

Dr. Lowy suggested that the NCAB submit a written statement to the NIH that outlines precisely the points that they want to convey. He also suggested contacting Dr. Michael Lauer (Deputy Director of Extramural Research, NIH) for helpful insight.

Clinical Trials Reporting, FDAAA (FDA Amendment Act) Final Rule, and NIH Policy Update
Dr. Sheila A. Prindiville, M.D., M.P.H.

Dr. Sheila A. Prindiville, Director, Coordinating Center for Clinical Trials, Office of the Director, NCI, provided an overview of the new requirements for clinical trial reporting through ClinicalTrials.gov. She reviewed the terms of the FDA Amendment Act of 2007 and outlined the NIH policies on reporting. The final rule of 2016 included the following:

- A request for further clarification of the FDAAA, especially the statutory language describing evaluation criteria for studies.
- An expansion of transparency of clinical trial reporting beyond statutory requirements.
- A requirement that the NIH post submitted information within 30 days of receipt regardless of whether the trial meets NIH quality-control review.

All these changes are designed to enhance understandability of results in the database of each clinical trial. For the FDAAA final rule requirement, the study start date is January 18, 2017.

She explained that under the new NIH policy, NOT-OD-16-149 (effective date January 18, 2017), dissemination of NIH-funded clinical trial information now includes behavioral and phase 1 trials. This applies to trials funded in whole or in part through either NIH extramural or intramural programs.

Dr. Prindiville raised two important points: First, these NIH policies apply to all trials, regardless of phase. Second, the final rule gives the NIH authority to withhold funding for clinical trials that are noncompliant with policy procedures.

She presented results reporting compliance data that showed a low and variable compliance rate. Compliance depended in part on to the type of sponsor (i.e., NIH versus industry). The level of compliance was not tightly associated with the award amount.

She summarized her presentation by stating that the overall goal of the reporting requirement is to increase transparency of results from clinical trials. The high-level implications for the recent policies include transparency, accountability, and leadership.

Discussion

Dr. Adamson commented that there is a real budget associated with this reporting, but currently there are no resources for reporting. The discrepancies in reporting may be unrelated to compliance, but rather due to limited funding. He concluded that the committee must engage in work soon to weigh in on potential unintended consequences of these requirements.

Dr. Lowy commented that this requirement represents a substantial change and recommended that the NCAB point out the potential negative consequences of the new policy changes. Dr. Abrams said that difficulty arises because the NIH is applying these changes to all trials.

Dr. Judy Garber asked whether the NCI will respond to all reports and whether it is prepared to handle the volume of reporting. She also wondered if there will be categories of grants that will allow for trials that are not a specified type. Dr. Abrams agreed with her assessment regarding reporting volume and added that reporting will not be viewed in real time. He mentioned that this is not a Request for Applications: Investigators have freedom with the type of science, but they will have to meet the reporting requirements.

Dr. Bruner requested that the respective missions for the NCI CTAC (Clinical Trials Advisory Committee) and the Clinical Investigations Subcommittee be presented before the next meeting. Dr. Adamson agreed with the suggestion.

Adjournment

Dr. Peter Adamson adjourned the Subcommittee meeting at 7:30 p.m. EST.